REMEDY FOR PNEUMOCYSTOSIS.CARINII PNEUMONIA

Patent Number: JP3240727
Publication date: 1991-10-28
Inventor(s): MATSUMOTO YOSHITSUGU
Applicant(s): TOYO JOZO CO LTD
Requested Patent: JP3240727
Application Number: JP19900034470 19900215
Priority Number(s):
IPC Classification: A61K31/41
EC Classification:
Equivalents:

Abstract

PURPOSE:To obtain the subject remedy, containing a specific compound such as aculeacins and capable of exhibiting more effective treating effects than those of the well-known drug with hardly any side effects. CONSTITUTION:A remedy containing a compound expressed by the formula (R1 is H or OH; R2 is 14-18C saturated or unsaturated fatty acid residue) as an active ingredient. Aculeacin Aalpha (R1 is OH; R2 is myristic acid residue), aculeacin Agamma (R1 is OH; R2 is palmitic acid residue), aculeacin Dalpha (R1 is H; R2 is myristic acid residue), echinocandin B (R1 is OH; R2 is linoleic acid residue), echinocandin C (R1 is H; R2 is stearic acid residue), etc., are cited as the compound expressed by the formula. The dose of the compound expressed by the formula is within the range of 10mg to 2g for an adult per day.

⑲日本国特許庁（JP）　⑪特許出願公開

⑫公開特許公報（A）　平3－240727

⑤1Int. Cl.⁵	識別記号	庁内整理番号
A 61 K 31/41	ACD	7475－4C
	AEB	7475－4C
// C 07 D 487/14		7019－4C
C 12 P 17/18	B	8931－4B
(C 12 P 17/18		
C 12 R 1:725)		

⑬公開　平成3年(1991)10月28日

審査請求　未請求　請求項の数 2　（全5頁）

⑤4発明の名称　ニューモシスチス・カリニ肺炎治療剤

⑳特　願　平2－34470
㉒出　願　平2(1990)2月15日

⑦2発明者　松本　芳嗣　京都府京都市北区大宮東脇台町16番地
⑦1出願人　東洋醸造株式会社　静岡県田方郡大仁町三福632番地の1

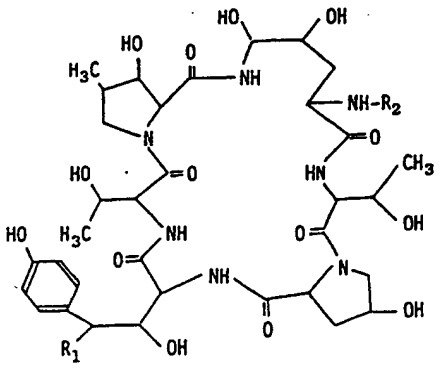
明細書

1．発明の名称

ニューモシスチス・カリニ肺炎治療剤

2．特許請求の範囲

1）一般式



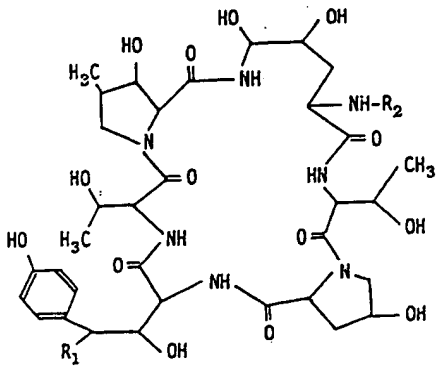
（式中、R_1は水素原子または水酸基を示し、R_2は炭素数14～18個の飽和または不飽和脂肪酸残基を示す）で表される物質を有効成分として含有することを特徴とするニューモシスチス・カリニ肺炎に対する予防または治療剤。

2）R_1が水酸基、R_2がミリスチン酸残基を示す物質、R_1が水素原子、R_2がミリスチン酸残基を示す物質、R_1が水酸基、R_2がパルミチン酸残基を示す物質またはR_1が水素原子、R_2がパルミチン酸残基を示す物質である請求項第1項記載のニューモシスチス・カリニ肺炎に対する予防または治療剤。

3．発明の詳細な説明

＜産業上の利用分野＞

本発明は、一般式



（式中、R_1は水素原子または水酸基を示し、R_2は炭素数14～18個の飽和または不飽和脂肪酸残基を示す）で表される物質を有効成分とするニューモシスチス・カリニ肺炎に対する予防または治療剤に関する。

＜従来の技術＞

ニューモシスチス・カリニ（Pneumocystis carinii）は分類学上の位置に議論のあるものの、原虫の一種であるとされており、現在までに1属1種が知られている。

このものが肺炎の病原体となり得ることが知られており、先天性免疫不全または栄養不良による低免疫力乳幼児、急性リンパ球性または骨髄性白血病などの小児疾患、高年齢層の自己免疫疾患、肺癌を主とする悪性腫瘍の場合、また特に抗腫瘍剤、ステロイド、免疫抑制剤を多量に使用した場合、またはＡＩＤＳ、トキソプラズマ、サイトメガロウィルス、放線菌、真菌類などの感染症と合併すると、ニューモシスチス　カリニ肺炎を発生し、呼吸不全によって死亡することが多い。

現在、ニューモシスチス・カリニ肺炎に対する有効性が報告されている薬剤としては、抗菌剤であるスルファメトキサゾールとトリメトプリムとの配合剤（ＳＴ合剤）および抗原虫薬であるペンタミジンが報告されているが、サルファ剤はＡＩＤＳ患者に対して毒性が強く、またペンタミジンはそれ自体毒性が強いので、それらの使用が制約され、それに伴い治療効果も制限されている。

ニューモシスチス・カリニの確認方法として、菌子をアニリン・ブルーまたはゴモリ（Gomori's）メテナミン銀で染色する方法などが知られている〔Workshop on Pneumocystis carinii, 21S, 1988〕。

アクレアシンＡα、アクレアシンＡγ、アクレアシンＤα、アクレアシンＤγなどの抗生物質アクレアシン類はアスペルギルス・アクレアタスＭ4845により生産され、キャンジダ・アルビカンスなどの酵母類の増殖を阻止し、皮膚糸状菌や植物病原糸状菌などの糸状菌に対して増殖抑制作用を有することが知られており〔特公昭59－20350～3号公報〕、これらのアクレアシン類と化学構造上極めて類似する類縁物質として抗糸状菌抗生物質エキノキャンディンＢおよびＣも知られている〔Tetrahedron Letters, 4147－4150（1976）、Helv. Chim. Acta, 62（4）, 1252－1267（1979）〕が、これらの物質がニューモシスチス・カリニ肺炎の治療剤として使用できることについては何ら報告されていない。

＜発明が解決しようとする問題点＞

上述の如く、ニューモシスチス・カリニ肺炎の治療には特殊な薬剤を用いる必要があり、その有効性が報告されているが、その使用が限定されている。

従って、副作用が少なく、より有効な治療効果を示すニューモシスチス・カリニ肺炎治療剤の出現が望まれている。

＜問題点を解決するための手段＞

かかる実情において、本発明者は、ニューモシスチス・カリニ肺炎治療剤としてより有効な治療効果を示す物質について種々検索した結果、全く意外にも抗生物質アクレアシンＡα、Ａγ、Ｄαやγなどの前記一般式で表される物質が、実験的ラットのニューモシスチス・カリニ肺炎モデルにおいて有効な予防および治療効果を示すことを見出し、本発明を完成したものである。

即ち、本発明は、前記一般式（式中、R_1は水素原子または水酸基を示し、R_2は炭素数14～18個の飽和または不飽和脂肪酸残基を示す）で表される物質を有効成分として含有することを特徴とするニューモシスチス・カリニ肺炎に対する予防または治療剤である。

上記の有効成分としては、前記一般式で表される物質であり、例えば公知の抗生物質アクレアシン類、エキノキャンジン類が挙げられる。

アクレアシン類の例としては、アクレアシンＡα（R_1＝ＯＨ、R_2＝ミリスチン酸残基：C14）、アクレアシンＡγ（R_1＝ＯＨ、R_2＝パルミチン酸残基：C16）、アクレアシンＤα（R_1

＝H、R₂＝ミリスチン酸残基：C14）、アクレアシンDγ（R₁＝H、R₂＝パルミチン酸残基：C16）が挙げられ、それらの製造法については特公昭59－20350、同59－20351、同59－20352、同59－20353号公報などに記載されている。

エキノキャンジン類の例としては、エキノキャンジンB（R₁＝OH、R₂＝リノール酸残基：C18:2）、エキノキャンジンC（R₁＝H、R₂＝ステアリン酸残基：C18）が挙げられ、それらの製造法については、Tetrahedron Letters, 4147－4150（1976）、Helv. Chim. Acta, 62（4）, 1252－1267（1979））に記載されている。

本発明の有効成分は、公知の賦形剤、結合剤、溶解剤、崩壊剤、滑沢剤、コーティング剤、その他適当な添加剤と共に公知の製剤技術に従って種々の剤形、例えば錠剤、カプセル剤、散剤、顆粒剤、シロップ剤、ドライシロップ剤、噴霧剤などの剤形とすることができる。

また、公知の安定剤、溶解補助剤、緩衝剤、等張化剤、乳化剤、無痛化剤、その他適当な添加剤と共に公知の注射剤調製技術に従って注射剤とすることができる。

さらにまた、公知の坐剤基剤、その他適当な添加剤と共に公知の坐剤調製技術に従って坐剤とすることができる。

本有効成分は水に難溶性であるので、注射剤とする場合には、例えば、注射用蒸留水にデオキシコール酸ナトリウム、その他の医薬用に使用可能な界面活性剤、低級アルコールなどの公知の溶解補助剤（場合により公知の安定剤、緩衝剤、pH調節剤などを適宜含有させてもよい）を溶解し、その溶液に本有効成分、マンニトール、グルコースなどの等張化剤、その他適当な添加剤を溶解した後、除菌フィルターに通して無菌化したものをバイアル壜に分注し、凍結乾燥することにより調製される。用時、注射用蒸留水等で溶解して注射剤とすればよい。

本有効成分は、経口投与にあるいは非経口投与のいずれの投与形態でもよいが、非経口投与する場合には、静脈注射による投与あるいは坐剤による直腸投与が好ましい。

本有効成分の投与量は、一般的には、成人1日当り10mg～2g程度であり、患者の症状、体重、投与経路などの相違に応じて適宜増減すればよい。

本有効成分のマウスに対する急性毒性（LD_{50}, mg／kg）について、デオキシコール酸ナトリウムを溶解補助剤として調製した有効成分水溶液を使用して，そのLD₅₀を求めた。その結果は第1表の通りである。

第1表　LD_{50}（mg／kg）

有効成分	投与経路	LD_{50}
アクレアシンAα	静脈内	350
〃	筋肉内	600
アクレアシンAγ	静脈内	350
アクレアシンAγ	筋肉内	600
アクレアシンDα	筋肉内	＞1000
アクレアシンDγ	筋肉内	＞1000

＜発明の効果＞

次に、抗ニューモシスチス・カリニ作用について述べる。

Sprague－Dawley（SD）ラット（1群3匹）にプレドニゾロン（1匹当り5mg）を週2回づつ皮下投与し、テトラサイクリン（10000mg／ℓ）を飲料水中に投与した。このような状態で55日間飼育するとニューモシスチス・カリニ肺炎を自然発症させることができる。

上記の状態で本有効成分を投与しない未投与群とプレドニゾロン投与と同時に本有効成分を1匹当り10mg／kgの割合で週2回づつ腹腔内に投与した群とを飼育した。

両投与群について上記条件下に55日間飼育した後に屠殺し、剖検後、肺についてホルマリン固定後、組織切片を作製し、嚢子壁を染色するゴモ

リ・メテナミン銀染色手段により染色されるニューモシスチス・カリニ肺炎に特徴的な嚢子を、1000倍の顕微鏡下100視野当りの嚢子数を計測した。嚢子数の減少で有効性を判定した。その結果は第2表の通りである。

第2表

ラットNo	投与薬物 投与量（mg／kg）	嚢子数
1	対照群（未投与群）	1878
2	〃	5547
3	〃	1497
4	アクレアシンAr 10	578
5	〃	446
6	〃	503
7	アクレアシンDr 10	150
8	〃	33
9	〃	0
1	対照群（未投与群）	1878
2	〃	5547
3	〃	1497
10	アクレアシンAr 50	0
11	〃	130
12	〃	0

上記の結果から、プレドニゾロン投与開始後、2週間後からアクレアシンAr50mg／kgを週2回づつ投与した結果、55日後では嚢子数平均43個であり、対照群（未投与群）（嚢子数平均2947個）と比し明らかな減少を認めた。

尚、本有効成分投与群の肺は肉眼的にはいずれも明らかな異常を認めず、対照群に比し明らかに良好な状態を示した。同様にアクレアシンAα、Dα、Drについても同様の結果が得られた。

また、上記の飼育条件下に本有効成分の未投与群と1匹当り2．5mg／kgの割合で週2回づつ腹腔内に投与した群を飼育した結果、2．5mg／kg投与群においては未投与群に比し著しい

上記の結果から、アクレアシンAr10mg／kgを週2回づつ投与した結果、55日後では嚢子数平均509個であり、対照群（未投与群）（嚢子数平均2947個）と比し明らかな減少を認めた。

また、アクレアシンDr10mg／kgを週2回づつ投与した結果でも、55日後では嚢子数平均61個であり、対照群（嚢子数平均2947個）と比し、明らかな減少を認めた。

上記の試験において、プレドニゾロン投与開始後、2週間後から本有効成分を1匹当り50mg／kgの割合で週2回づつ腹腔内に投与した群を同時に飼育した。55日後に屠殺し、上記と同様の方法で嚢子数を計測し、嚢子数の減少で有効性を判定した。その結果は第3表の通りである。

第3表

ラットNo	投与薬物 投与量（mg／kg）	嚢子数

延命効果が認められた。

以上の通り、本有効成分はニューモシスチス・カリニの嚢子の増殖を抑制することから、ニューモシスチス・カリニ肺炎に対する予防または治療剤として有用である。

＜実施例＞

次に、本有効成分の製剤例を挙げるが、これにより本発明を限定するものではない。

実施例 1

注射用製剤

デオキシコール酸ナトリウム25gを注射用蒸留水5lに溶解し、これにアクレアシンAr100gおよびマンニトール100gを溶解した後に除菌フィルターに通して除菌した。この溶液をバイアル瓶に5mlづつ分注し、これらを凍結乾燥して注射用製剤を得た。

用時、注射用添付液に溶解して投与する。

実施例 2

注射用製剤

実施例1において、アクレアシンArの代わり

にアクレアシンDγを用いて注射用製剤を得た。

実施例　3

注射用製剤

実施例1において、アクレアシンAγの代わりにアクレアシンAαを用いて注射用製剤を得た。

実施例　4

注射用製剤

実施例1において、アクレアシンAγの代わりにアクレアシンDαを用いて注射用製剤を得た。

特許出願人

東洋醸造株式会社

代表者　高田　哲男

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 589 074 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
21.11.2001 Bulletin 2001/47

(51) Int Cl.[7]: **A61K 31/70**, A61K 33/06

(21) Application number: **92116154.3**

(22) Date of filing: **22.09.1992**

(54) **Carbohydrate complexes for destruction of resistant cancer cells**

Kohlenhydrate-Komplexe zur Vernichtung von Krebszellen

Complexes d'hydrates de carbone pour la destruction de cellules cancéreuses

(84) Designated Contracting States:
CH DE FR GB IT LI SE

(43) Date of publication of application:
30.03.1994 Bulletin 1994/13

(73) Proprietor: **Takayanagi, Takeo, Dr.**
New York, N.Y. 10705 (US)

(72) Inventor: **Takayanagi, Takeo, Dr.**
New York, N.Y. 10705 (US)

(74) Representative:
Gille Hrabal Struck Neidlein Prop Roos
Patentanwälte
Brucknerstrasse 20
40593 Düsseldorf (DE)

(56) References cited:
EP-A- 0 431 736 **FR-A- 2 126 134**

- **PATENT ABSTRACTS OF JAPAN vol. 12, no. 122 (C-488)15 April 1988**
- **PATENT ABSTRACTS OF JAPAN vol. 16, no. 490 (C-994)12 October 1992**

EP 0 589 074 B1

Printed by Jouve, 75001 PARIS (FR)

Description

BACKGROUND OF THE INVENTION :

1. Field of the Invention

[0001] The present invention relates to novel saccharide complexes for the treatment of resistant cancer.

2. Related Art

[0002] Cancer has been a fatal disease since the year 300 B.C.

[0003] Cancer cells generally constitute a divergent and mixed population, and among said population there are survivor cells (0.1-2%), which are resistant against all forms of treatment. If a cell escapes it will multiply rapidly to a trillion cells in 20 years. Accordingly, cancer seems to be incurable, and chemically resistant cancer cells are not probable.

[0004] An effective treatment of cancer cells was described in JP-A- 62 242 658 by the direct combination of a substance with biological activity, like for instance a carcinostatic agent or an antiobiotic agent with a specific azo compound.

[0005] Products with cytostatic activity are described in FR-A-2 126 134, such products consisting of cyclophosphamide in combination with another compound, in particular with an inorganic magnesium derivative. The combination displays an improved cytostatic activity.

[0006] Cyclodextrins are described in EP-A- 0 431 736 to be suitable for the treatment of diseases related with male hormones, like e.g. the treatment of a prostate enlargement

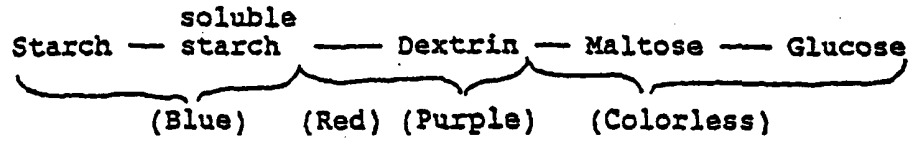
[0007] A composition suitable to prevent colon and rectal cancer has been described in JP-A- 41 79 459, the composition consisting of roasted dextrin with alpha-amylase and/or glycoamylase.

[0008] In the present state of affairs it appears that chemical synthesis and the medical treatment of cancer has not developed significantly and hereupon a study of advisable biologically active substances in vitro and in vivo has been undertaken.

[0009] During the study of a survivor cell membrane, a series of saccharide complexes that have remarkable anticancer abilities has been discovered. The result of the investigation has made it possible to anticipate the achievement of cancer therapy and may be designed to provide a clue to the solution of the problem.

[0010] In the present invention the common saccharides serve as the starting material hydrolyzed by acid or an enzyme. Also, commercially available saccharide esters or ethers are used for the same purpose.

[0011] The hydrolysis is carried out smoothly in a diluted HCl or H_2SO_4 solution to the extent of 7.5-15% of acid under heating or in an enzymic solution. Primarily, a fundamental criterion of the present hydrolysis type of starch and the harvest separation of ingredients are given in the following table.



[0012] The grades of the hydrolysis and the result of the color reaction with Iodine is partly divided. During the progressing reaction a starch-iodine reaction and microscopic observation of the destruction state of cancer cells should be continuously monitored. The most effective fraction strikes the end of slightly red color parts, and at that time the heating is stopped and the mixture is subjected to a powerful air-drying process. The resulting product is almost viscous.

[0013] The resulting product consists of stereospecific products that are extensively effective and do not necessarily separate the fractions.

[0014] The hydrolysed saccharide was dissolved in 2-methoxyethanol in the presence of a further component which produces the specific destructing effect on the cancer cells and is characterised hereafter as reinforcing agent or cell destructive factor.

It is necessary according to the invention to add a magnesium compound to the solution of the modified saccharide, such magnesium compound being magnesium sulfate.

[0015] It is possible to provide the saccharide by subjecting a carbohydrate compound which is itself only slightly soluble to acetolysis as displayed in the following table.

The Table of acetolysis				
Specimen of saccharides	Composition after acetolysis			Heating Times (Decomposition product)
	Acetic anhydride	Acetic acid	Sulfuric acid	
Cellulose	10	10	1	30°C, 2 days (Simple saccharide), 5 days (Cellobiose)
Dextran	8	5.3	1	30°C, 7 days after 7 days 80 °C. 30 min. Hirclose
"	8	5.3	1	After acetylation 40°C. 30 min. (Trisaccharides)
Mannan	10	10	1	After acetylation 40°C. 13 hr.
Glycopeptide	10	10	1	20°C. 1 - 4 days (Simple Polysaccharides)

[0016] Several drops of the mixture are diluted with water. Lugol reagent is added to this solution, and the color reaction and a microscopic test are simultaneously carried out to determinate the most effective part. Saccharide ester is also available for the same purpose. The esterification of saccharides is easily carried out in a usual manner. Should satisfactory hydrolysates be found, the enzymic hydrolysis products may be added by another.

[0017] The enzymes play an important role in anaerobic energy production by supplying steric oxidation. When the study of hydrolysis continued, it was confirmed that the cyclodextrin also has a remarkable anticancer ability, and it was first introduced to the present invention.

[0018] The cyclodextrin was discovered just over 100 years ago (1891) by Vielliears. It was studied in detail and the following polymorphic forms of steric compounds have been chromatographically isolated and identified.

α-,β-,γ-,∈-,δ-,ζ-,η-,θ- cyclodextrin

[0019] These compounds are important as a chemical for the study of host and guest chemistry.

[0020] According to the present invention, the preparation of the most chemotherapeutically effective saccharide compounds are accomplished in a solvent, particularly in ethylene glycol monomethyl ether, accompanying a 1-3 destruction factor. The condensation occurs by a magnesium sulfate solution owing to the electrostatic attraction, wherein the included components are indiscriminately in a liquid or a solid state. This was confirmed in all our experiments and a related method has hitherto not been published.

[0021] As above described, cancer cells constitute a mixed population, whereas a single effective agent cannot penetrate the significant resistance of the cancer cells. Cancer cells have a remarkable ability to cope with a wide range of external environments. Further, many difficulties arise during cancer therapy and it is most troublesome that there is a total number of 60 species of cells. Naturally a large number of competitors are required.

[0022] In general, carbohydrates (saccharide) are accepted as an important mobile carrier of metabolically available energy source in the cells. Indeed, the several hydroxyl groups in the compounds are favorably located and their mechanism accounts for the catalytic effect. The carbohydrates can be hydrolyzed by acid or an enzyme and they provide excellent material for a selected investigation. Furthermore, they are highly acceptable to cyclization (acylation), acetylation, alkylation and esterification in the usual manner.

[0023] The applied factors are prepared as follows. The amino compounds and amino acid group are easily obtained by kneading with various metal oxydes adding a small quantity of water as a friction polymer. The diazonium salts of the same are effective and are stabilized in clathrate compounds, or the diazonium salts easily form additional complexes. The metal fixed enzymes are easily applied to the present invention.

[0024] Pursuing a solution to the mechanism of resistance of cancer cells to discover the cause of said resistance. The autolysis phenomenon necessitates a small amount of metal salts and from the clue noted in the text the following compounds were provided experimentally:

$I(ZnCl_2)$, $Cu(NH_4)_2\ Cl_4$, $I(CuCl_2)$,

$I(CaCl_2)$ and other metal salts.

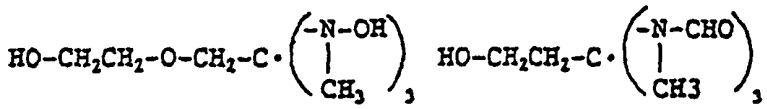
Furthermore, as organic substances, the following compounds would occur to be suitable

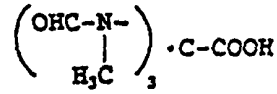
tert-$(CH_3)_3CC_6(OH)_2$, $C_4H_2N_2O_4$,

p-$C_6H_4O_2$, $C_{10}H_6O_2$, $(CH_3)_3CC_6H_3(OH_3)OH$. Since these results suggest the stimulation of an exhaustive screening of the inorganic or organic compounds.

[0025] A great number of random screening tests have been effected and the results are present in the following data.

$I(ZnCl_2)$-NN-$CH_2COOC_2H_5$, tert-$(CH_3)_3CC_6H_3(OH)_2$ $I(CaCl_2)$-NN-$CH_2COOC_2H_5$, $I(CuCl_2)$-NHC_6H_3(OH) COOH, HNHNOCNH_4C_6, CaN$COOC_2H_5$, $I(CaCl_2)$, CaN-$CH_2COOC_2H_5$, Na_2 CH_2 $COOC_2H_5$, $Cu(NH_4)_2Cl_4$, HONHCONH_2, Mg:NCH_2CH_2Br, 1,4-$C_{10}H_6O$-NCONHCH_2CH_2-OH, HONHCO$CH_2C_2NH_2$, C_5H_4N-$CONHNH_2$, 1,4-$C_{10}H_6O$: N-$CH_2COOC_2H_5$, p-C_6H_4O-$NCH_2COOC_2H_5$ · 6-$C_5H_3N_4$-N:N-$CH_2COOC_2H_5$, I $(CuCl_2)$ -NN-$CH_2COOC_2H_5$, Hg: NCH_2CH_2Br, Cu: NCH_2CH_2Cl Hg:$NCH_2CH_2SO_3H$, -NN-C_6H_3 (OH) COOH, -N: N-OS-NH (CH_2:$CHCH_2$), $C_4H_2N_2O_3$: N-$COOC_2H_5$





or ester Schweizer reagent, -N:N-$CH_2CH_2SO_3H$, -N:N-$CH_2COOC_2H_5$, $(CH_3)_3CC_6H_3(OCH_3)OH$, $(CH_3)_3CO_6H_3(OH)_2$:N:N-$CH_2COOC_2H_5$.

[0026] Chemotherapy may be defined as the selective destruction of pathogenic organisms within a host by chemical agents. The attempt to resolve the cancer problem was unsuccessful. The fate of the drugs was traced by using the following Table.

[0027] Cell destruction % after 10Mn. after 5-7 days on an ascites mouse easily goes up to the following

+	++	+++	++++	V	VI
30%	60%	90%	98%	99.9%	100%

falls under the category of survivor, the survivor invades the tissue.

[0028] Even the best drug barely goes to 98% and prolongs life. 99.9% of the mice experience 30% complete recovery after injection. 0.1-0.001% will correspond to strong survivor cells, which should be destroyed in 10 minutes for complete recovery. At present there is no approach to the long standing cancer problem.

At the time of cell destruction, microscopic observation is excellent, forming glittering bubbles and twinkling all over under reflected sunlight. The same phenomenon occurs by using safety match powder.

[0029] At last, laboratory synthesis of survivor cell destruction complexes have been achieved by the substitution of several OH functional groups in the saccharide hydrolysates with the following radicals:

NaSH, $NaNH_2$, $NaOCH_3$, NaF, NaN_3 and $NaBH_4$.

[0030] These complexes can wipe out the resistant cancer survivor cells thoroughly without reinforcing agents. The disappearance of cancer cells is presumably a result of the increased enzymic function of the saccharide hydrolysate, because a radical change is strengthened by the fact that all molecules have one pair of electrons. This fact may hold the key to the solution of long standing cancer problem.

[0031] The saccharide complexes have the advantage that the intended effective agents can be included within the complexes, liquid substances will be pulverized, malodorous active agents will be deodorized, insoluble material will be easily water soluble and have high stability.

[0032] Furthermore, it is now substantiated that this invention has the advantage of obtaining many effective substances through adequate variation and combination of the substituents and the condensation components. Finally numerous new effective compounds necessary for combination therapy against resistant viruses have been found.

[0033] The new complex-compound of this invention has accurate inhibitory properties against the growth of tissue, therefore the complexes are available for the treatment of malignant tumors or to inhibit new formations. The related experiment has been carried out since the year 1968 and is now under the support of the National Cancer Institute of America.

[0034] The compounds of this invention are, as mentioned above, nearly not toxic, tasteless, stimulusless and odorless and furthermore have no side effects and are water soluble. Therefore, this hybrid is widely applicable for clinical use.

[0035] In the following examples there are described several preferred embodiments to illustrate the invention.

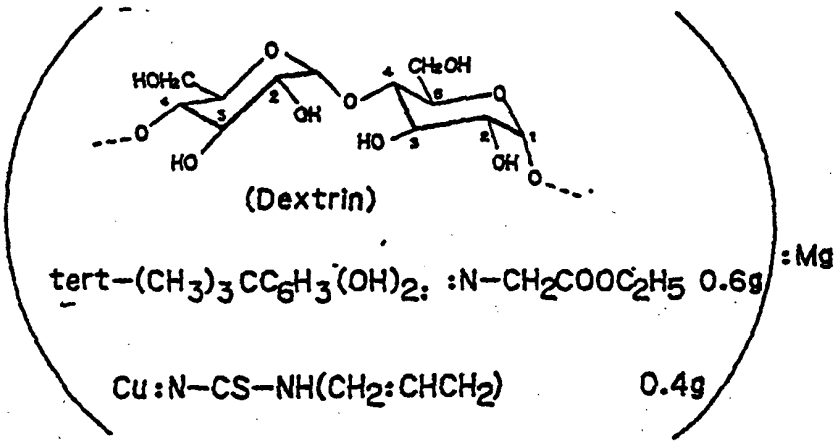
Example 1

[0036] 2% of starch was dissolved in 40 ml of a 7.5% HCl solution for almost 15 min. and heated in a water bath. The time-course of heating was followed with a resulting starch-iodine color reaction and simultaneous observation of cell destruction stated microscopically in the ascites. The most effective part of this case corresponds to the end of the red part in the table indicated. Then the mixture was poured into the water, and was neutralized with barium carbonate and the resulting product was separated. The product was taken out and was dissolved in a 40 ml 2-methoxyethanol mixture with a 1 : 1/2 ratio reinforcing agent selected from the above cited group that is appropriate to the intended cancer species

tert-$(CH_3)_3CC_6H_3(OH)_2$:N-$CH_2COOC_2H_5$

Cu:N-CS-NH(CH_2:CH-CH_2)

[0037] Then into the mixture was poured the concentrated magnesium solution with vigorous stirring until the solution completely coagulated. The product was washed with petroleum ether and air-dried on filter paper to obtain an easily water soluble complex that decomposed at 180°C. The resulting complex has the following formula.



Example 2

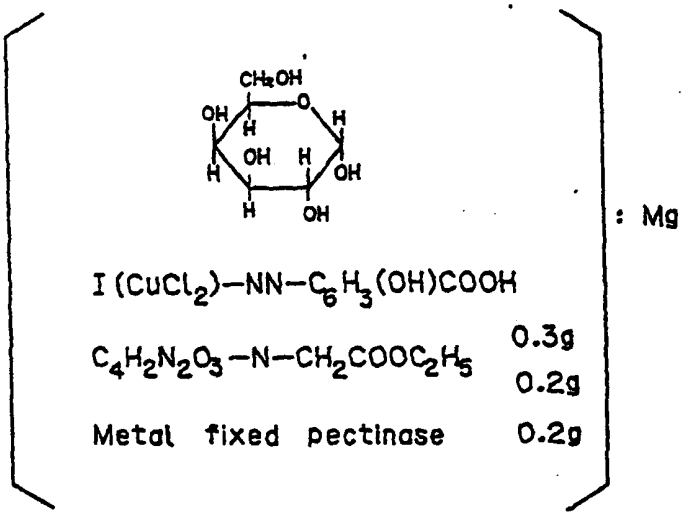
[0038] 1 g of milk sugar was dissolved in 40 ml of a 7.5% HCl solution about 10 Min. and heated in a water bath. The time of heating may lead to a determination regarding the state of cell destruction. Then the mixture was poured into the water and was neutralized with barium carbonate and the resulting product was separated. The hydrolysates were taken out and the solution was dissolved in 50 ml of 2-methoxyethanol, and the following reinforcing agents were added into the mixture

I($CuCl_2$)-NN-C_6H_3(OH) COOH

$C_4H_2N_2O_3$-N-$CH_2COOC_2H_5$

Metal fixed pectinase.

[0039] Successively undergoes electromagnetic condensation with concentrated $MgSO_4$ solution. The resulting product was air-dried on a filter paper and has the following structural formula:



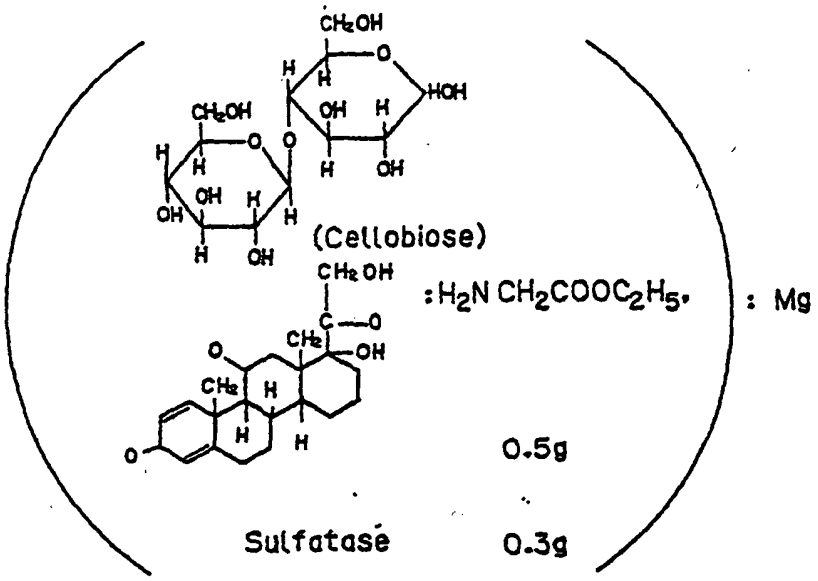
Example 3

[0040] 2g of cellulose were added portionwise into the mixture of the following acid:

Acetic anhydride	17 ml
Acetic acid	17 ml
Sulfuric acid	1.8 ml

and cooled and then the mixture should be allowed to stand 7 days at 25°C-30°C. Finally it should be heated at 80°C for 30 Min.

[0041] The mixture was then was poured into the water. It was neutralized with sodium carbonate and the aqueous mixture was extracted with chloroform. The extract was dried under reduced pressure and the resulting acetyl products are subjected to deacetylation in the usual manner. Further manipulation should be done exactly according to the previously outlined procedure. The following formula of the product was subsequently provided.

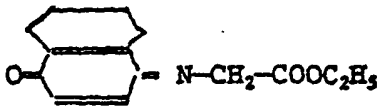


Example 4

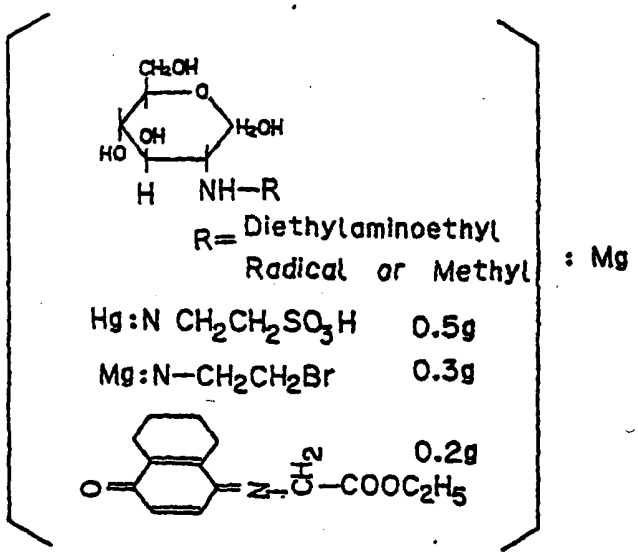
[0042] 2 g of N-Diethylaminoethyl D-Glucosamine were dissolved in 40 ml of 2-methoxyethanol and then the reinforcing agents

Hg:N-$CH_2CH_2SO_3H$

Mg:N CH_2CH_2Br



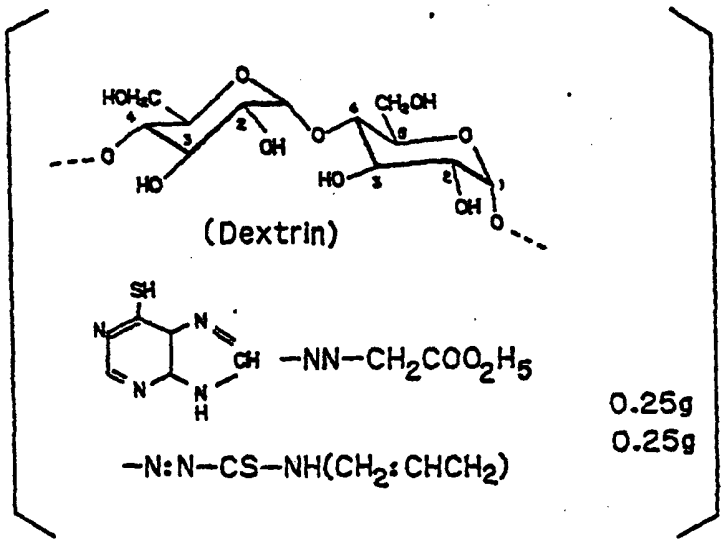
were added to the mixture. Successively, a concentrated magnesium sulfate solution was poured into the mixture until it completely coagulated. The resulting product was taken out and subjected to air-drying on the filter paper to obtain an water soluble complex which decomposed at 180°C and the resulting complex has the following structural formula:



Example 5

[0043] 1 g Starch(2.3 μmol) was added to β-Galactosidase, (8.0.unit), 0.05 citric acid puffer solution, pH4.0, 0.6 ml into a moderate quantity of water and the mixture was allowed to stand at 37°C for 15 hr. The product secured comprises various ambiguous steric saccharides.

[0044] Then the mixture was filtrated and the reinforcing agent in the ratio of 1 : 1/2 was added into the mixture and it was allowed to stand at room temperature overnight. Then 50 ml 2-methoxyethanol was added into the mixture and successively underwent magnesium condensation. The resulted coagulum is air-dried on filter paper. According to this invention the used enzyme may feasibly vary by changes in experimental conditions. The resulting complex is water soluble and has the following structural formula:



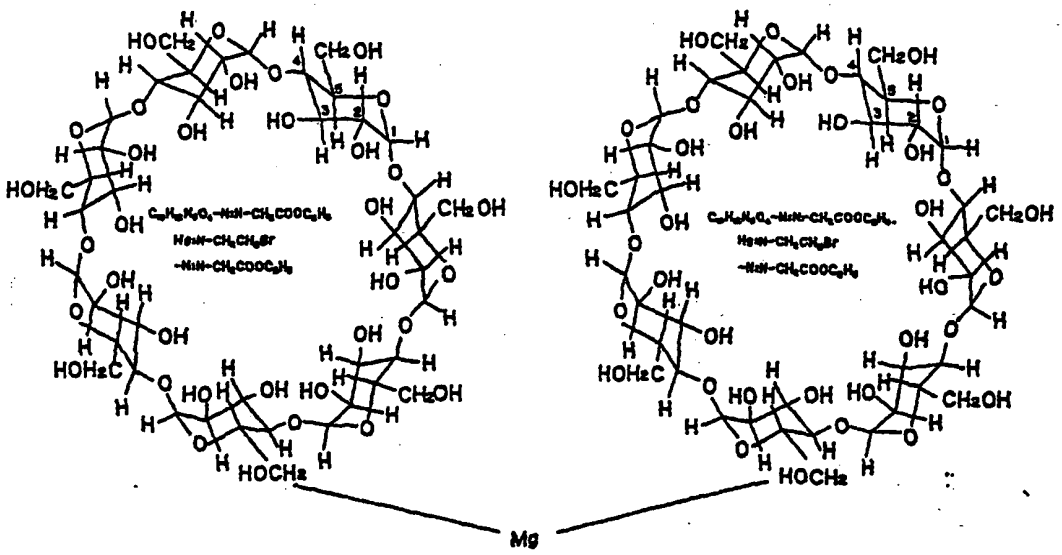
Example 6

[0045] The chemicals α-, β-, γ- cyclodextrin were first introduced in the present invention with extraordinary effect regarding cancer chemotherapy. These compounds are used individually or mixed, moreover with adequate destruction agents in 2-methoxyethanol by condensing agent $MgSO_4$ coagulation of the solution was brought about.

[0046] For preparation of the complex, 2 g β-cyclodextrin was dissolved in 60 ml of 2-methoxyethanol and then as a reinforcing agents

$C_{10}H_{12}N_5O_4$-N:N-$CH_2COOC_2H_5$	0.7 g
Hg:N-CH_2CH_2Br	0.7 g
-N:N-$CH_2COOC_2H_5$	0.1 g

were added to the mixture. Successively, a concentrated magnesium solution was poured into the mixtures until it completely coagulated. The resulting product was taken out and subjected to air-drying, which has the following structural formula:

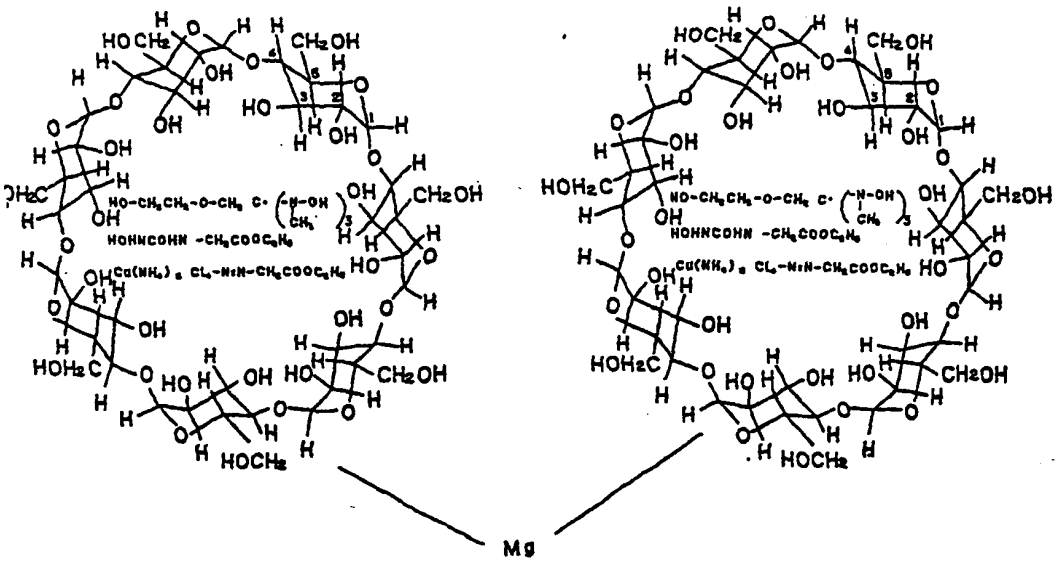


Example 7

[0047] For preparation of the new saccharide complex 2 g of α-, β-, γ- cyclodextrin (individually or mixed) were dissolved in 60 ml methoxyethanol and then the reinforcing agents

$HO-CH_2CH_2-O-CH_2C\cdot\left(\begin{matrix}-N-OH\\ \vert\\ CH_3\end{matrix}\right)_3$	0.5 g
HOHNCOHN $-CH_2COOC_2H_5$	0.2 g
$Cu(NH_4)_2\ Cl_4$-N:N-$CH_2COOC_2H_5$	0.2 g

were added to the mixture. Successively, a concentrated magnesium sulfate solution was poured into the mixture until it completely coagulated. The resulting product, which was taken out and subjected to air-drying, has the following structural formula:

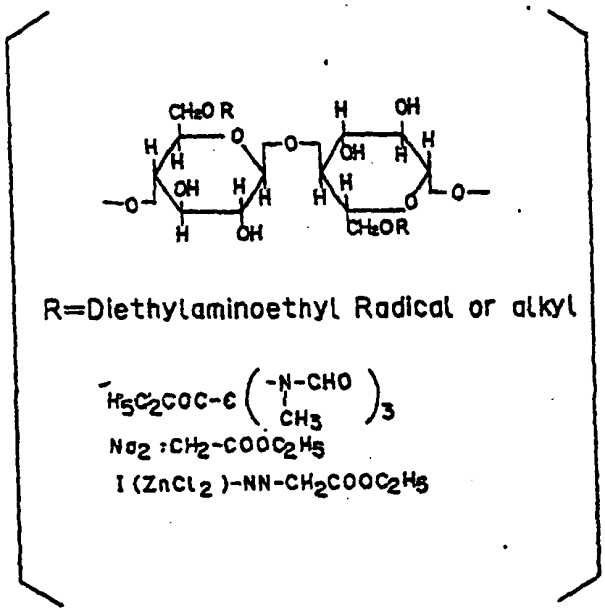


Example 8

[0048] For preparation of the saccharide complex, 2 g of Diethylaminoethyl Cellulose were dissolved in 60 ml 2-methoxyethanol and then the reinforcing agents

$H_5C_2OOC-C\cdot\left(\begin{matrix}-N-CHO\\ \vert\\ CH3\end{matrix}\right)_3$	0.5 g
$Na_2\ CH_2\ COOC_2H_5$	0.2 g
$I(ZnCl_2)-NN-CH_2COOC_2H_5$	0.2 g

were added to the mixture. Successively, a concentrated magnesium sulfate solution was poured into the mixture until it completely coagulated. The resulting product, which was taken out and subjected to air-drying, has the following structural formula:



Example 9

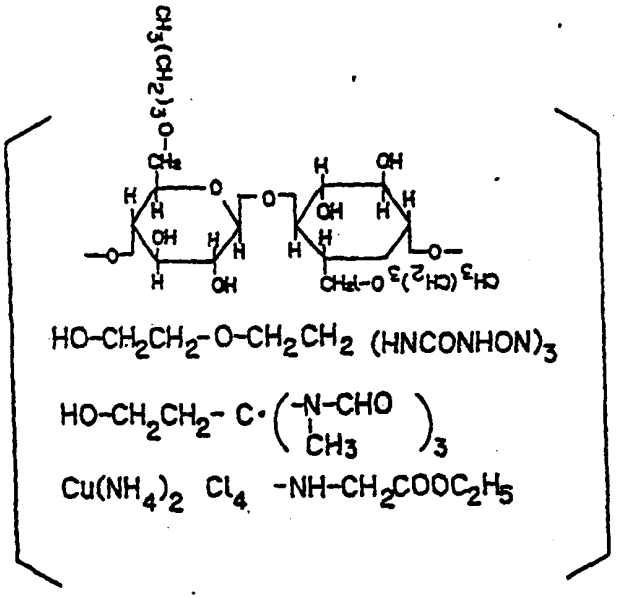
[0049] For preparation of the new saccharide complex 2 g of Butyl-cellulose was dissolved in 60 ml 2-methoxyethanol and then the reinforcing agents

$HO-CH_2CH_2-O-CH_2CH_2(HNCONHON)_3$ 0.5 g

$HO-CH_2CH_2-C\left(\begin{matrix}-N-CHO\\ |\\ CH_3\end{matrix}\right)_3$ 0.4 g

$Cu(NH_4)_2\ Cl_4\ -NH-CH_2COOC_2H_5$ 0.1 g

were added to the mixture. Successively, a concentrated magnesium sulfate solution was poured into the mixture until it completely coagulated. The resulting product, which was taken out and subjected to air-drying, has the following structural formula:

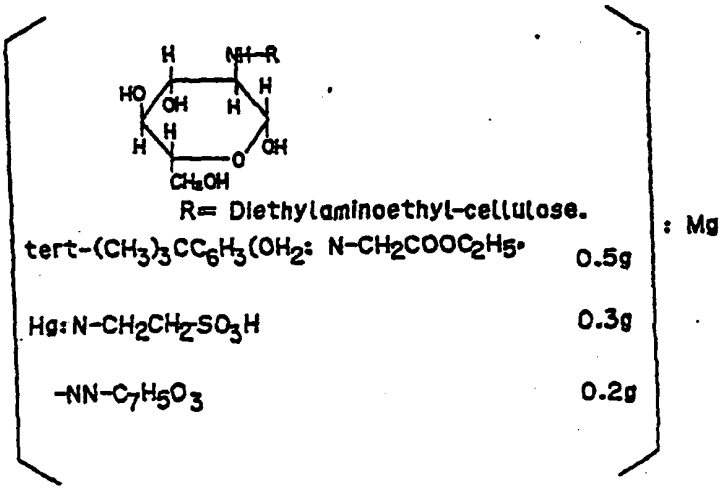


Example 10

[0050] For preparation of the new saccharide complex, 2 g of Diethylaminoethyl-D-glucosamine were dissolved in 60 ml of 2-methoxyethanol and then the cell destruction factors

tert-$(CH_3)_3CC_6H_3(OH_2$:N-$CH_2COOC_2H_5$, 0.5 g
Hg:M-CH_2CH_2-SO_3H
-NN-$C_7H_5O_3$

were added to the mixture. Successively, a concentrated magnesium sulfate solution was poured into the mixture until it completely coagulated. The resulting product, which was taken out and subjected to air-drying, has the following structural formula:

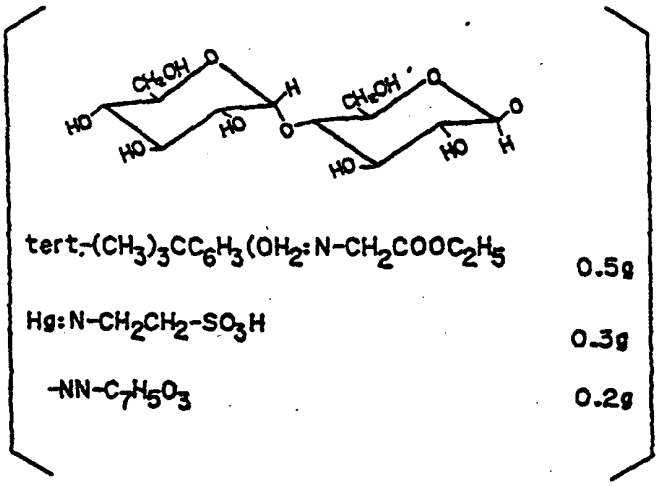


Example 11

[0051] For preparation of the new saccharide complex, 2 g of β-D-Mannose were dissolved in 60 ml 2-methoxyethanol and then the destruction factors

tert-$(CH_3)_3CC_6H_3(OH_2$:N-$CH_2COOC_2H_5$,
Hg:N-CH_2CH_2-SO_3H
-NN-$C_7H_5O_3$

were added to the mixture. Successively, a concentrated magnesium sulfate solution was poured into the mixture until it completely coagulated. The resulting product, which was taken out and subjected to air-drying, has the following structural formula:



Example 12

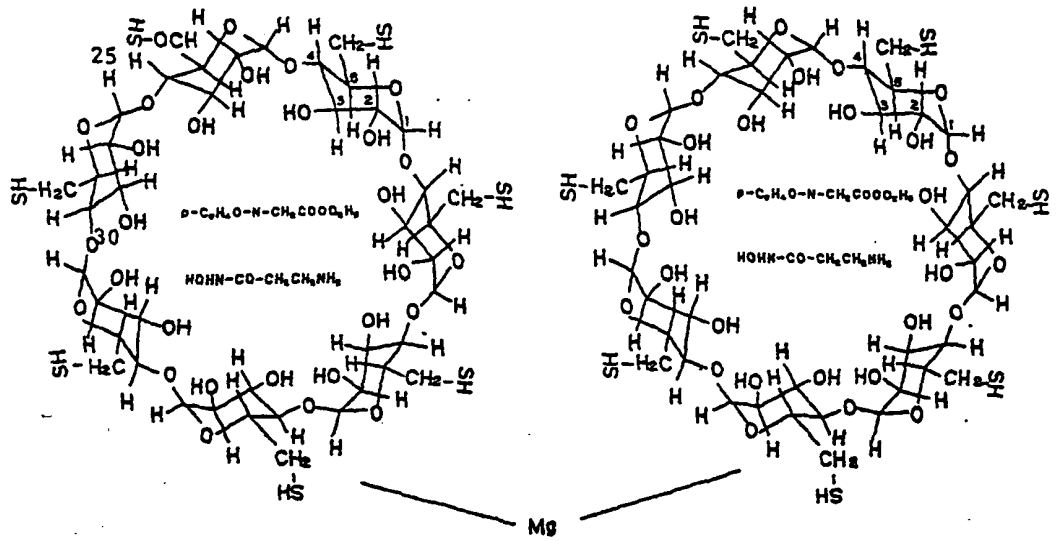
[0052] For preparation of the new saccharide complex 2 g of α-, β-, γ-cyclodextrin (individually or mixed) were dissolved in 60 ml of 2-methoxyethanol and then a 20 ml of Hydrogen Sulfide (NaSH) solution added to the mixture. A simultaneous reaction occurs with the rise of temperature, it then becomes cloudy and very soon a flocculent precipitate separates out from the solution. Wherein, the following sodium compounds:

$NaNH_2$, NaN_3, NaF, Na-OCH_3, $NaBH_4$

were used instead of NaSH for a similar reaction. A precipitate was dissolved in 60 ml of 2-methoxyethanol, if necessary, and

p-C_6H_4O-N-$CH_2COOO_2H_5$ 0	0.6 g
HOHN-CO-$CH_2CH_2NH_2$	0.4 g

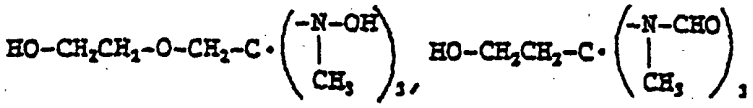
added to the mixture and then underwent magnesium sulfate condensation. The resulting coagulum, which dried on a filter paper, has the following structural formula:

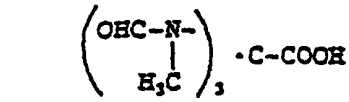


Claims

1. A process for the production of a chemotherapeutically useful saccharide complex, comprising the steps of:

   hydrolysing a saccharide with an enzyme or an acid;
   dissolving the saccharide in 2-methoxyethanol together with a further compound, selected from the group consisting of
   I ($ZnCl_2$)-NN-$CH_2COOC_2H_5$, tent- $(CH_3)_3CC_6H_3(OH)_2$ I($CaCl_2$)-NN-$CH_2COOC_2H_5$, I($CuCl_2$)-NHC_6H_3(OH) COOH, HNHNOCNH_4C_6, CaN$COOC_2H_5$, I($CaCl_2$), CaN-$CH_2COOC_2H_5$, Na_2 CH_2 $COOC_2H_5$, Cu$(NH_4)_2Cl_4$, $HONHCONH_2$, Mg:NCH_2CH_2Br, 1,4-$C_{10}H_6$O-NCONHCH_2CH_2-OH, $HONHCOCH_2CH_2NH_2$, C_5H_4N-$CONHNH_2$, 1,4-$C_{10}H_6$O:N-$CH_2COOC_2H_5$, p-C_6H_4O-N$CH_2COOC_2H_5$. 6-$C_5H_3N_4$-N:N-$CH_2COOC_2H_5$, I ($CuCl_2$)-NN-$CH_2COOC_2H_5$, Hg:NCH_2CH_2Br, Cu:NCH_2CH_2Cl Hg:N$CH_2CH_2SO_3H$, -NN-C_6H_3 (OH) COOH, -N: N-CS-NH(CH_2:$CHCH_2$), $C_4H_2O_3$:N-$COOC_2H_5$





   or ester, Schweizer reagent, -N:N-$CH_2CH_2SO_3H$, -N:N-$CH_2COOC_2H_5$, Hg:N-CH_2CH_2Br $(CH_3)_3CC_6H_3(OCH_3)$ OH, and $(CH_3)_3CC_6H_3(OH)_2$:N:N-$CH_2COOC_2H_5$, and adding a $MgSO_4$ solution to the solution of the modified saccharide.

2. The process according to claim 1, wherein said hydrolysed saccharide is a saccharide ester or ether or a saccharide with at least one OH-group substituted with -SH, -NH_2, -O-CH_3,-N_3, -F or -BH_4.

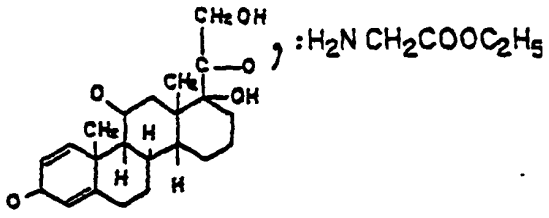
3. Process according to any of claims 1 or 2, wherein the saccharide complex comprises at least one compound

selected from the group consisting of α-cyclodextrin, β-cyclodextrin and γ-cyclodextrin.

4. Process according to claim 1 or 2, wherein the saccharide complex comprises tert- $(CH_3)_3CC_6H_3(OH)_2$:N-$CH_2COOC_2H_5$ and Cu:N-CS-NH(CH_2:CH-CH_2).

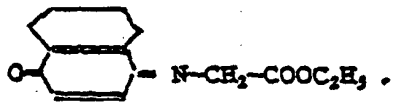
5. Process according to claim 1 or 2, wherein the saccharide complex comprises
$I(CuCl_2)$-NN-$C_6H_3(OH)COOH$,
$C_4H_2N_2O_3$-N-$CH_2COOC_2H_5$ and
Metal fixed pectinase.

6. Process according to claim 1 or 2, wherein the saccharide complex comprises

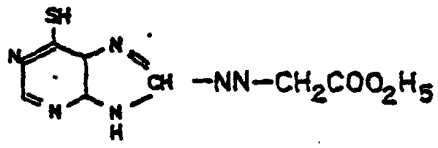


and Sulfatase.

7. Process according to claim 1 or 2, wherein the saccharide complex comprises
Hg:N-$CH_2CH_2SO_3H$,
Mg:N CH_2CH_2Br and



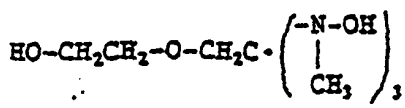
8. Process according to claim 1 or 2, wherein the saccharide complex comprises



and
-N:N-CS-NH(CH_2:$CHCH_2$).

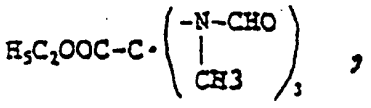
9. Process according to claim 3, wherein the saccharide complex comprises
$C_{10}H_{12}N_5O_4$-N:N-$CH_2COOC_2H_5$,
Hg:N-CH_2CH_2Br and
-N:N-$CH_2COOC_2H_5$.

10. Process according to claim 3, wherein the saccharide complex comprises



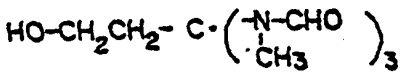
HOHNCOHN -$CH_2COOC_2H_5$ and
$Cu(NH_4)_2$ Cl_4-N:N-$CH_2COOC_2H_5$.

11. Process according to claim 1 or 2, wherein the saccharide complex comprises



Na_2 CH_2 $COOC_2H_5$ and
I ($ZnCl_2$) -NN-$CH_2COOC_2H_5$,

12. Process according to claim 1 or 2, wherein the saccharide complex comprises
HO-CH_2CH_2-O-CH_2CH_2 $(HNCONHON)_3$,



and
$Cu(NH_4)_2$ Cl_4 -NH-$CH_2COOC_2H_5$.

13. Process according to claim 1 or 2, wherein the saccharide complex comprises 13. Process according to claim 1 or 2, wherein the complex comprises
tert- $(CH_3)_3CC_6H_3(OH_2$:N-$CH_2COOC_2H_5$,
Hg:N-CH_2CH_2-SO_3H and
-NN-$C_7H_5O_3$.

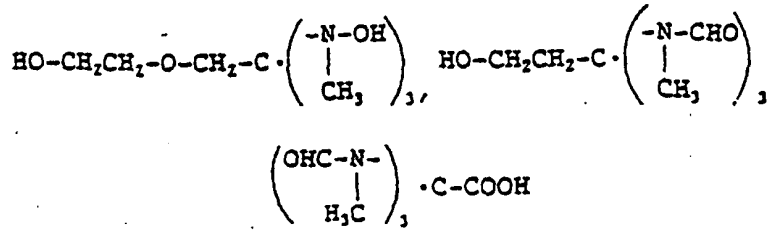
14. Process according to claim 1 or 2, wherein the saccharide complex comprises
tert- $(CH_3)_3CC_6H_3(OH_2$:N-$CH_2COOC_2H_5$,
Hg:N-CH_2CH_2-SO_3H and
-NN-$C_7H_5O_3$.

15. Process according to claim 3, wherein the saccharide complex comprises
p-C_6H_4O-N-$CH_2COOO_2H_5$ and
HOHN-CO-$CH_2CH_2NH_2$.

Patentansprüche

1. Verfahren zur Herstellung eines chemotherapeutisch einsetzbaren Saccharidkomplexes, umfassend die Schritte:

Hydrolyse eine Saccharids mit einem Enzym oder einer Säure;
Lösen des Saccharids in 2-Methoxyethanol gemeinsam mit einer weiteren Verbindung, die ausgewählt wird aus der aus
I ($ZnCl_2$) -NN-$CH_2COOC_2H_5$, tert- $(CH_3)_3CC_6H_3(OH_2)_2$ I ($CaCl_2$) -NN-$CH_2COOC_2H_5$, I ($CuCl_2$)-NHC_6H_3(OH) COOH, HNHNOCNH_4C_6, CaN$COOC_2H_5$, I($CaCl_2$), CaN-$CH_2COOC_2H_5$, Na_2 CH_2 $COOC_2H_5$, Cu $(NH_4)_2Cl_4$, HONHCONH_2, Mg: NCH_2CH_2Br, 1,4-$C_{10}H_6O$-NCONHCH_2CH_2-OH, HONHCO$CH_2CH_2NH_2$, C_5H_4N-$CONHNH_2$, 1,4-$C_{10}H_6O$:M-$CH_2COOC_2H_5$, p-C_6H_4O-N$CH_2COOC_2H_5$. 6 -$C_5H_3N_4$-N:N-$CH_2COOC_2H_5$, I ($CuCl_2$)-NN-$CH_2COOC_2H_5$, Hg:NCH_2CH_2Br, Cu:NCH_2CH_2Cl Hg:N$CH_2CH_2SO_3H$, -NN-C_6H_3 (OH)COOH, -N: N-CS-NH(CH_2:$CHCH_2$), $C_4H_2N_2O_3$:N-$COOC_2H_5$



oder Ester, Schweizer-Reagens, -N:N-$CH_2CH_2SO_3H$, -N:N-$CH_2COOC_2H_5$, Hg: N-CH_2CH_2Br $(CH_3)_3CC_6R_3$ $(OCH_3)OH$, and $(CH_3)_3CC_6H_3$ $(OH)_2$: N : N-$CH_2COOC_2H_5$

bestehenden Gruppe und Zugabe einer $MgSO_4$-Lösung zu der Lösung des modifizierten Saccharids.

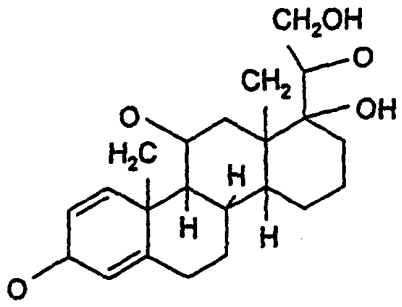
2. Verfahren nach Anspruch 1, wobei das hydolisierte Saccharid ein Saccharidester oder -ether oder ein Saccharid mit mindestens einer OH-Gruppe ist, die substituiert ist durch -SH, -NH_2, -O-CH_3, -N_3, -F oder -BH_4.

3. Verfahren nach einem der Ansprüche 1 oder 2, wobei der Saccharidkomplex mindestens eine Verbindung umfasst, die ausgewählt wird aus der aus α-Cyclodextrin, β-Cyclodextrin und γ-Cyclodextrin bestehenden Gruppe.

4. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex
   Tert-$(CH_3)_3CC_6H_3(OH)_2$:N-$CH_2COOC_2H_5$
   und Cu:N-CS-NH(CH_2:CH-CH_2)
   umfasst.

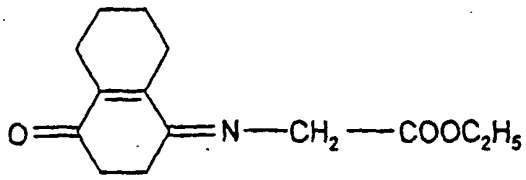
5. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex
   I($CuCl_2$)-NN-C_6H_3(OH) COOH,
   $C_4H_2N_2O_3$-N-$CH_2COOC_2H_5$
   und metallfixierte Pectinase
   umfasst.

6. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex



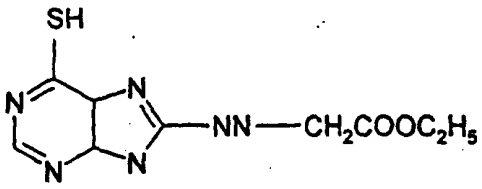
$H_2NCH_2COOC_2H_5$
und Sulfatase
umfasst.

7. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex
   Hg : N-$CH_2CH_2SO_3H$,
   Mg : N CH_2CH_2Br und



umfasst.

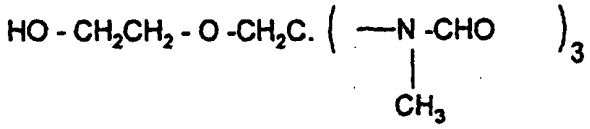
8. Verfahren noch Anspruch 1 oder 2, wobei der Saccharidkomplex



und -N:N-CS-NH(CH_2:$CHCH_2$)
umfaßt.

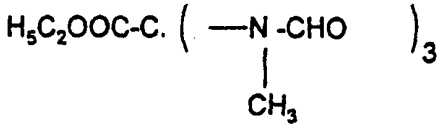
9. Verfahren nach Anspruch 3, wobei der Saccharidkomplex
$C_{10}H_{12}N_5O_4$-N-$CH_2COOC_2H_5$,
Hg:N-CH_2CH_2Br
und -N:N-$CH_2COOC_2H_5$
umfasst.

10. Verfahren nach Anspruch 3, wobei der Saccharidkomplex



HOHNCOHN -$CH_2COOC_2H_5$
und $Cu(NH_4)_2$ Cl_4-N:N-$CH_2COOC_2H_5$
umfasst.

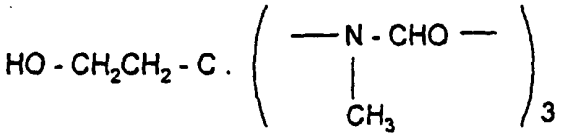
11. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex



$Na_2CH_2COOC_2H_5$

und $I(ZnCl_2)$-NN-$CH_2COOC_2H_5$
unfasst.

12. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex
$HO-CH_2CH_2-O-CH_2CH_2(HNCONHON)_3$,



und $Cu(NH_4)_2\ Cl_4$-NH-$CH_2COOC_2H_5$
umfaßt.

13. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex
Tert-$(CH_3)_3CC_6H_3(OH)_2$:N-$CH_2COOC_2H_5$
Hg:N-$CH_2CH_2SO_3H$
und -NN-$C_7H_5O_3$
umfasst.

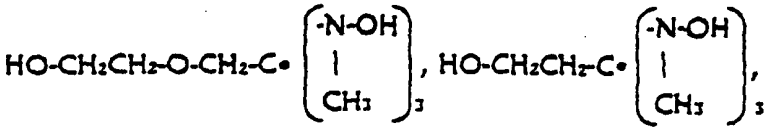
14. Verfahren nach Anspruch 1 oder 2, wobei der Saccharidkomplex
Tert-$(CH_3)_3CC_6H_3(OH)_2$:N-$CH_2COOC_2H_5$
Hg:N-$CH_2CH_2SO_3H$
und -NN-$C_7H_5O_3$
umfasst.

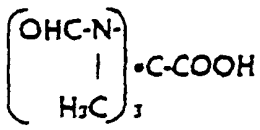
15. Verfahren nach Anspruch 3, wobei der Saccharidkomplex
p-C_6H_4O-N-$CH_2COOC_2H_5$
und HOHN-CO-$CH_2CH_2NH_2$
umfaßt.

Revendications

1. Procédé de production d'un complexe de saccharide utile du point de vue chimiothérapeutique, comprenant les étapes consistant :

- à hydrolyser un satcharide avec une enzyme ou un acide ;
- à dissoudre le saccharide dans du 2-méthoxyéthanol avec un autre composé, choisi dans l'ensemble consistant en :
$I(ZnCl_2)$-NN-$CH_2COOC_2H_5$, tert-$H_3(OH)COOH$, $HNHNOCNH_4C_6$, CaN-$COOC_2H_5$, $I(CaCl_2)$, CaN-$CH_2COOC_2H_5$, $Na_2CH_2COOC_2H_5$, $Cu(NH_4)_2Cl_4$, $HONHCONH_2$, Mg:NCH_2CH_2Br, 1,4-$C_{10}H_6O$-NCONHCH$_2$CH$_2$-OH, HON-HCOCH$_2$CH$_2$NH$_2$, C_5H_4-$CONHNH_2$, 1,4-$C_{10}H_6O$:N-$CH_2COOC_2H_5$, p-C_6H_4-$NCH_2COOC_2H_5$, 6-$C_5H_3N_4$-N:N-$CH_2COOC_2H_5$, $I(CuCl_2)$-NN-CH_2COO-C_2H_5, Hg:NCH_2CH_2Br, Cu:NCH_2CH_2Cl, Hg:$NCH_2CH_2SO_3H$, NN-C_6H_3(OH)-COOH, -N:N-CS-NH(CH_2:$CHCH_2$), $C_4H_2N_2O_3$:N-$COOC_2H_5$,





ou un ester, un réactif de Schweizer, -N:N-CH_2CH_2S-O_3H, -N:N-$CH_2COOC_2H_5$, Hg:N-CH_2CH_2Br, $(CH_3)_3CCH_3(OCH_3)OH$, et $(CH_3)_3CC_6H_5(OH)_2$:N:N-$CH_2COOC_2H_5$, et à ajouter une solution de $MgSO_4$ à la solution du saccharide modifié.

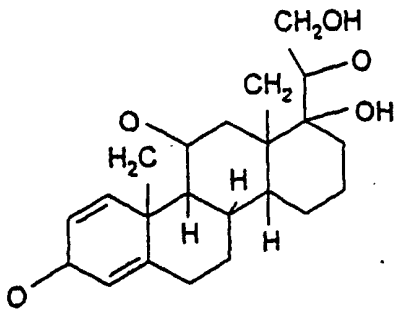
2. Procédé selon la revendication 1, dans lequel ledit saccharide hydrolysé est un ester ou un éther de saccharide ou un saccharide avec au moins un groupe OH substitué par -SH_2, -NH_2, -O-CH_3, -N_3, F ou -BH_4.

3. Procédé selon l'une quelconque des revendications 1 ou 2, dans lequel le complexe de saccharide comprend au moins un composé choisi dans l'ensemble constitué d'α-cyclodextrine, β-cyclodextrine et γ-cyclodextrine.

4. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend tert.-$(CH_3)_3CC_6H_3(OH_2)_2$: N-$CH_2COOC_2H_5$, et Cu:N-CS-NH-(CH_2:CH-CH_2).

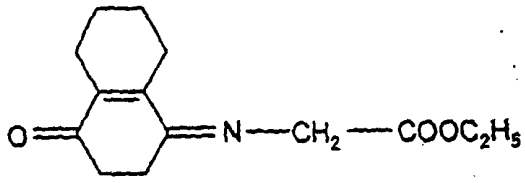
5. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend I($CuCl_2$)-N-C_6H_3(OH) COOH, $C_4H_2N_2O_3$-N-$CH_2COOC_2H_5$ et une pectinase fixée à un métal.

6. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend:

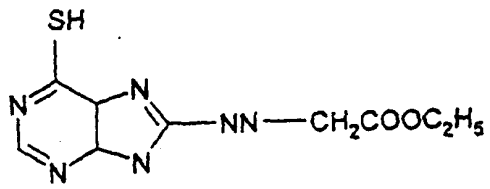


:$H_2NCH_2COOC_2H_5$ et une sulfatase.

7. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend Hg:N-$CH_2CH_2SO_3H$, Mg:N CH_2CH_2Br et



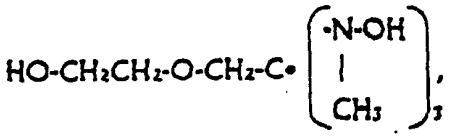
8. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend :



et-N:N-CS-NH(CH_2:$CHCH_2$).

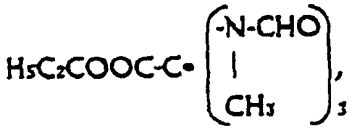
9. Procédé selon la revendication 3, dans lequel le complexe de saccharide comprend $C_{10}H_{12}N_5O_4$-N:N-$CH_2COOC_2H_5$, Hg:NCH_2CH_2Br et -N:N-CH_2C-OOC_2H_5.

10. Procédé selon la revendication 3, dans lequel le complexe de sacchande comprend:



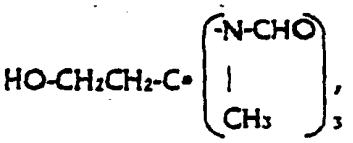
HOHNCOCH-$CH_2COOC_2H_5$ et Cu- $(NH_4)_2Cl_4$-N:N-$CH_2COOC_2H_5$.

11. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend :



$Na_2CH_2COOC_2H_5$ et I($ZnCl_2$)-NN-CH_2COO- C2H5.

12. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend : HO-CH_2CH_2-O-CH_2CH_2(HNCONHON)$_3$,



et $Cu(NH_4)_2Cl_4$-NH-$CH_2COOC_2H_5$.

13. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend tert.-$(CH_3)_3CC_6H_3(OH)_2$: N-$CH_2COO_2H_5$, Hg:N-CH_2CH_2-SO_3H et NN-$C_7H_5O_3$.

14. Procédé selon la revendication 1 ou 2, dans lequel le complexe de saccharide comprend tert.-$(CH_3)_3CC_6H_3(OH)_2$: N:N-$CH_2COO_2H_5$, Hg:N-CH_2CH_2-SO_3H et NN-$C_7H_5O_3$.

15. Procédé selon la revendication 3, dans lequel le complexe de saccharide comprend p-C_6H_6O-N-$CH_2COOC_2H_5$ et HONH-CO-$CH_2CH_2NH_2$.